



Peeling Back the Layers

A Case Based Trip Around the Cornea

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Disclosures

• Lang

- Allergan
- Avellino
- Aldeyra
- Dompe'
- Kala
- Novartis
- AOS
- Scope
- Sun Pharma
- Tarsus
- Quidel
- Horizon
- Aerie
- Ocular Therapeutix
- Orasis
- Oyster Point





Respond at [Pollevo.com/jacoblant676](https://www.pollevo.com/jacoblant676)

Text **JACOB LANG676** to **22333** once to join, then **A, B, C, or D**

Cornea World Tour

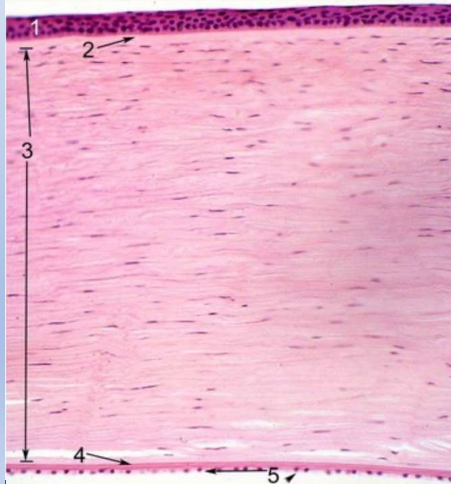
• *Learning Objectives:*

- *To better understand therapeutic options for corneal and ocular surface disease as well as their advantages and disadvantages.*
- *To recognize how these specialized layers interact to create this amazing optically clear tissue known as the cornea.*
- *To explore the layers of the cornea and to understand how dysfunction and anatomy intersect to form pathology*



Cornea World Tour

Normal corneal anatomy: review



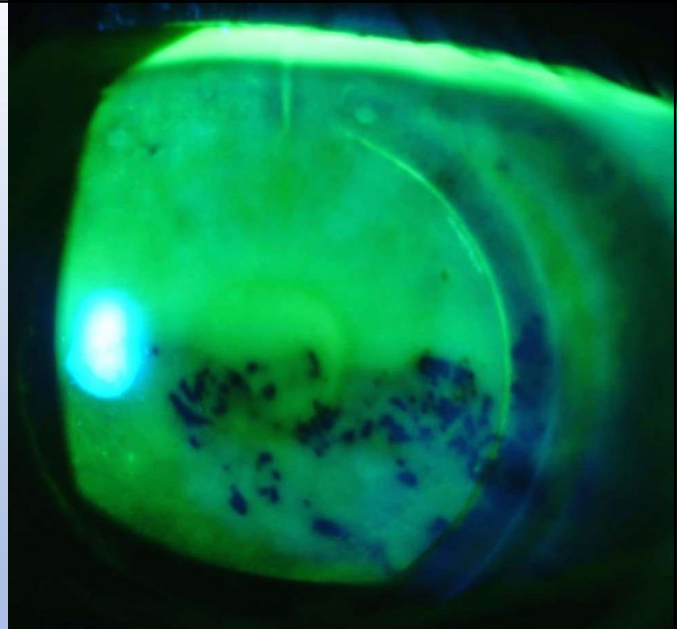
Layer	Approx thick	Approx Depth	Characteristics
Epithelium	50um	0-50um	Regular cellular structures
Corneal subbasal nerves			
Bowman's	10um	50-60um	Acellular granular appearance
Stroma	~460um	60-520um	Keratinocytes with visible nuclei (bright, ovoid), minimal cellular process visible
Descemet's	8-10um	520-530um	Acellular, fine granular appearance
Endothelium	5-6um	530-535um	Large, hexagonal shaped cells





Tear Film

- *Give credit where credit is due!*
- Refracting surface
- Bathes, nourishes, protects the Cornea



Tear Film

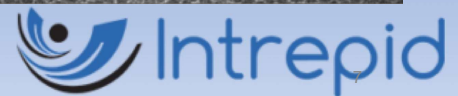
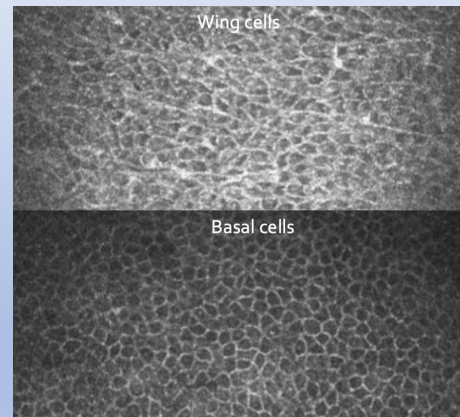
- Mucoaqueous layer:
 - 1500+ proteins
 - Electrolytes
 - Enzymes
- Lipid Layer
 - 100 microns
 - Prevents Evaporation
 - Seals the Deal





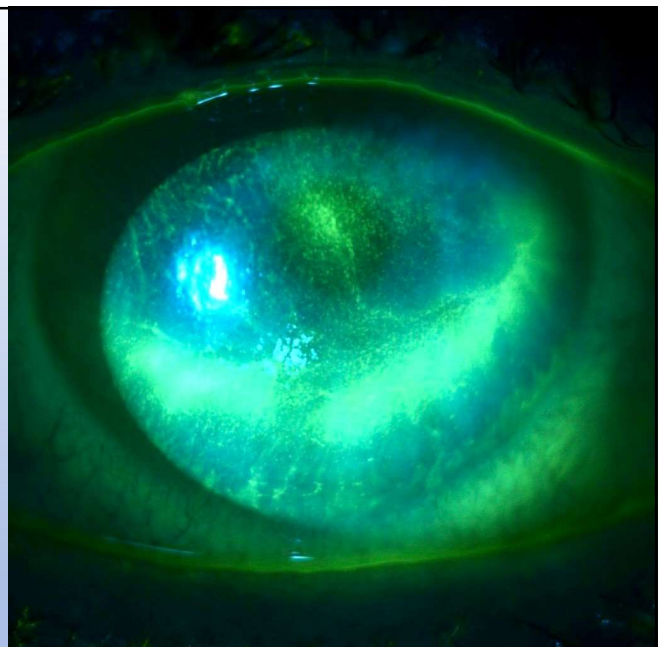
Epithelium

- **The corneal epithelial layers**
 - *Three or four layers of flattened squamous cells*
 - *Two or three layers of polyhedral cells, commonly known as wing cells*
 - *Basal epithelial cells where hemidesmosomes attach to the underlying basement membrane*
 - *Central thickness of corneal epithelium is approximately 50 μ m*



Epithelium

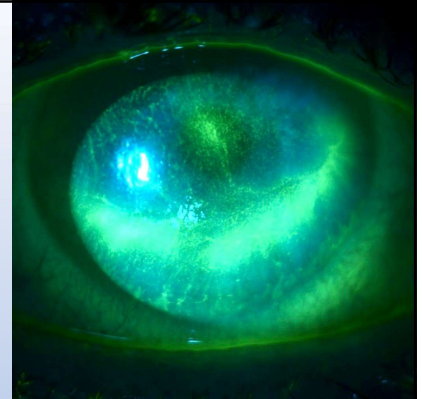
- *70 yo WM CC "Blurry Vision."*
- *2 weeks after uneventful cataract surgery*
- *With Istent*
- *Taking Ocuflax, Ketorolac, Pred Acetate*
- *Also trying Alaway, Naphcon, and something by Similasan*





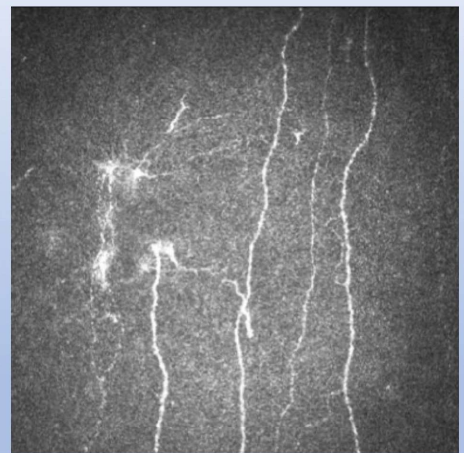
Epithelium

- *When assessing, think of...*
- *SPK Patterns, Location (where), and DDX(why)*
- *Corneal “attackers”*
- *Most innervated and therefore sensitive layer*
- *Does Pain and Stain “align”...why not?*
- *Pain vs Stain discussion*



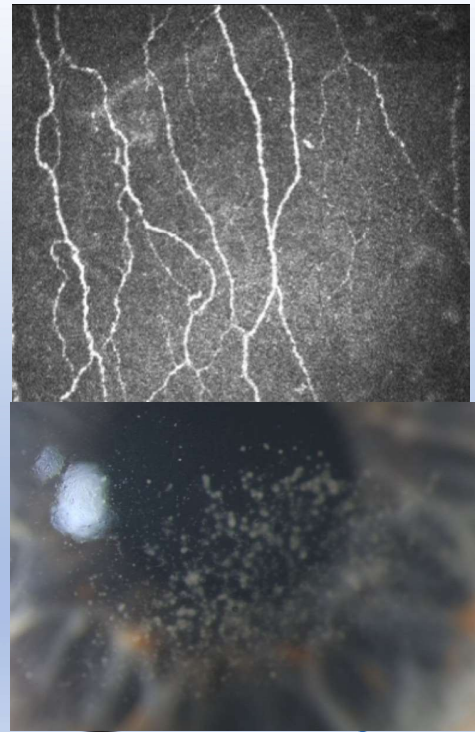
SGH Case

- *Patient presenting for DEEval*
- *Pain in LE x 4 years, chronic*
- *No PEK or lissamine green staining of conj*
- *1+ MGD*
- *TBUT 7-8 seconds both eyes*
- *She reports having dry eyes for “years” but LE has worsened significantly*
- *No history of infection or known trauma*
- *CBE: Right eye – 4.5cm central; Left eye – 6cm central*
- *Proparacaine Challenge Left: 6 => 1*





- Sub-basal nerve plexus:
- Provides trophic support to epithelium
- Epithelium provides support to nerves
- Sentinel system for homeostasis
- Sentinel system for immune system activation
- Dysfunction: likely leads to disconnect of symptoms v signs
- "Pain without stain" => neuropathic
- "Stain without pain" => neurotrophic



Epithelium

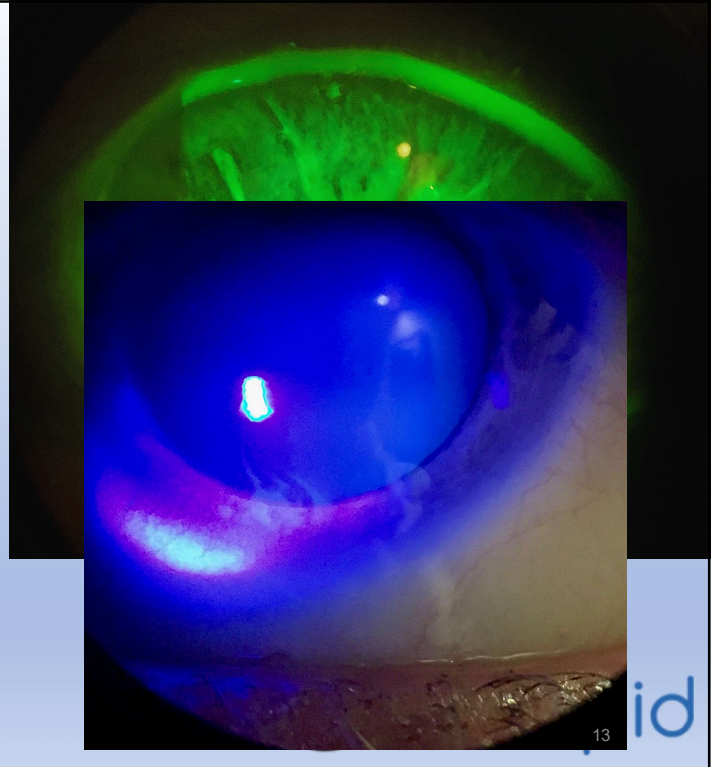
- Treatment Options:
- Lubrication
- Tear Preservation
- Immunomodulation
- "Regenerative" support
- Protection





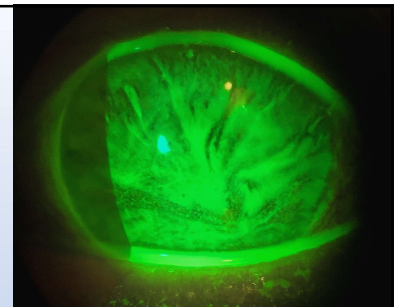
Epithelium

- 75 yo OSD consult
- Multiple surgeries, Glaucoma, Retina, Cataract, More Glaucoma...
- CC; Dry eyes and blurred vision



Epithelium

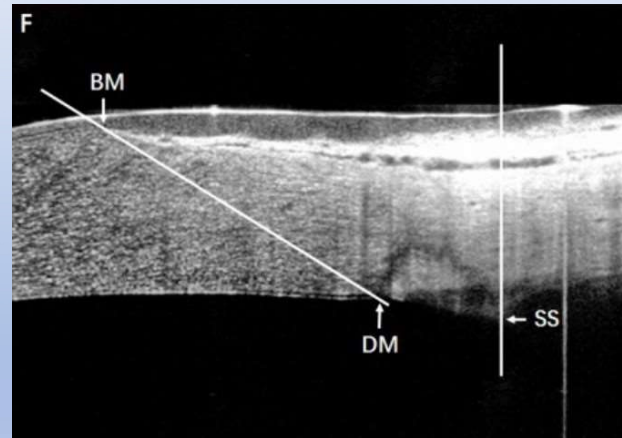
- *Limbal Stem Cell Deficiency*
- Diagnosis is primarily clinical
- Whorl pattern epitheliopathy
- Sectoral
- Usually starts superiorly (inferior in toric contacts?)
- Corneal haze/neovascularization





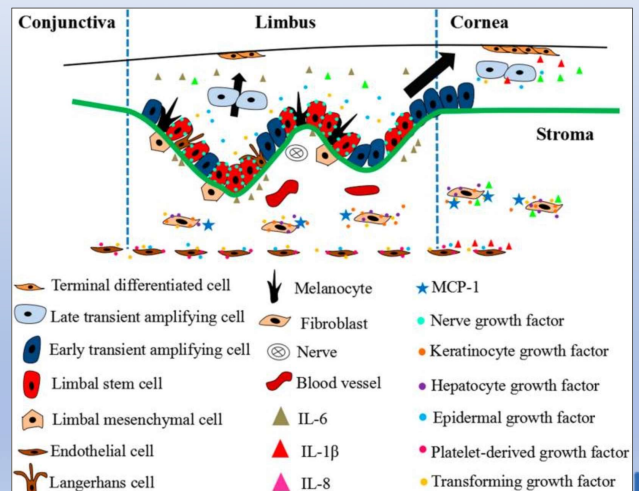
Anatomy of the Limbus

- *Definition: border between cornea and sclera*
- *Histology:*
- *Anterior: line between ending of Bowmans membrane and Descemet's membrane*
- *Posterior: perpendicular line from scleral spur, relative to external surface of the globe*



Anatomy of the Limbus

- *LSC's only account for a small number of cells in the limbal region*
- *TACs*
- *Melanocytes*
- *Langerhan's cells*
- *Basement membrane*
- *Vascular / neurological components*



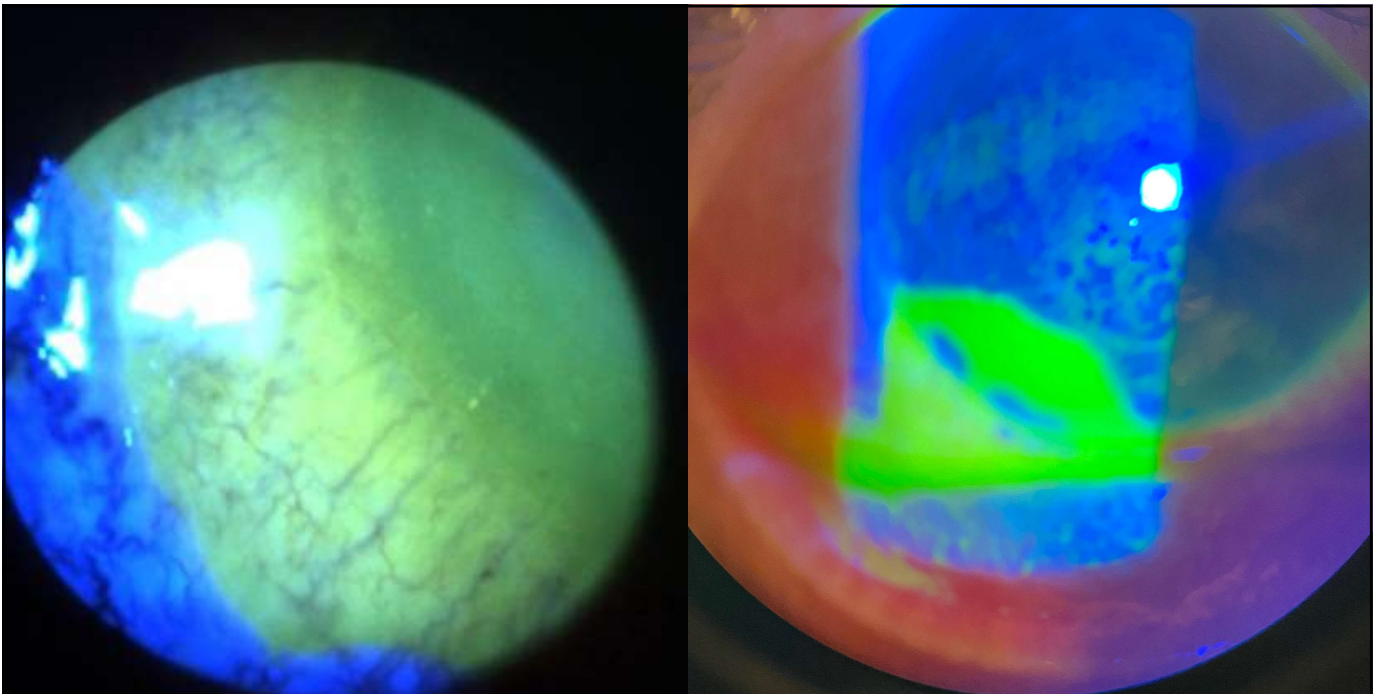
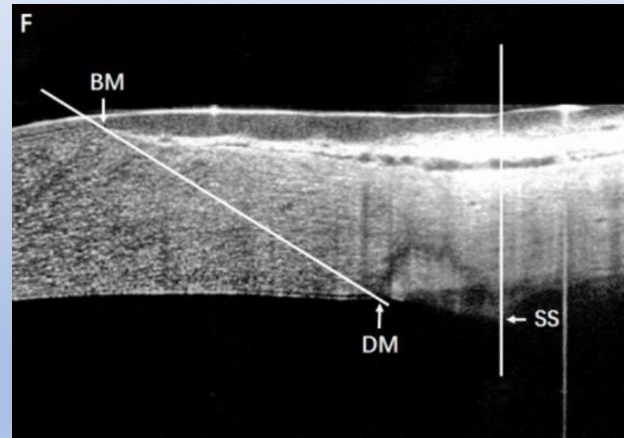


Factors affecting Limbal Stem Cell Niche

- *Inflammation and trauma*
- *Cytokines and Growth Factors:*

- *TGF-B3*
- *bFGF*
- *VEGF*
- *PDGF*
- *NGF*

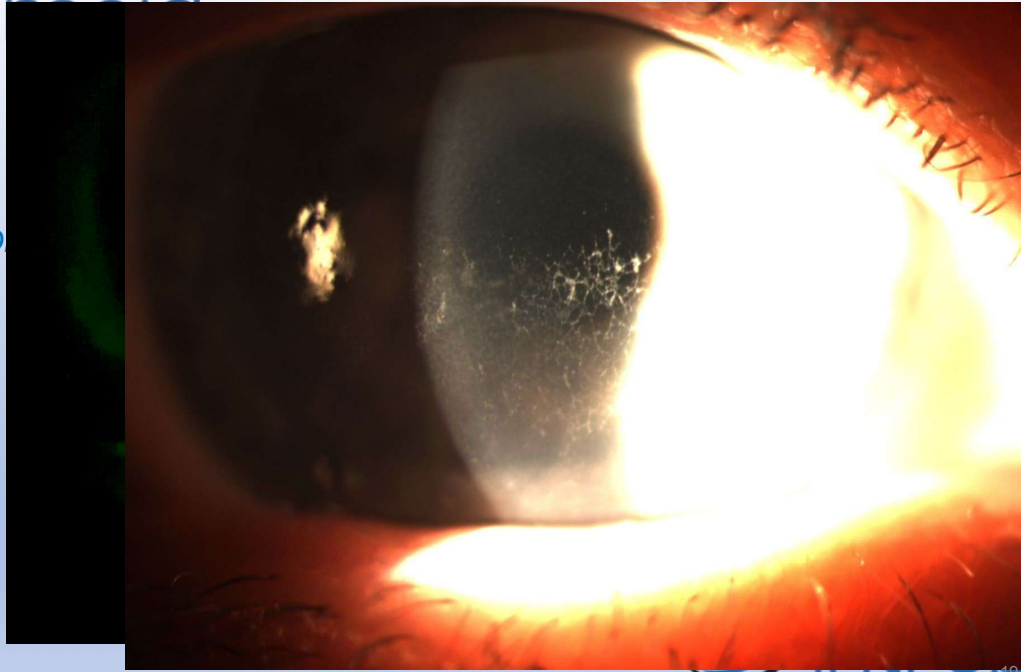
- *Substrates present in the LSCN*
- *Collagen*
- *N-cadherin*



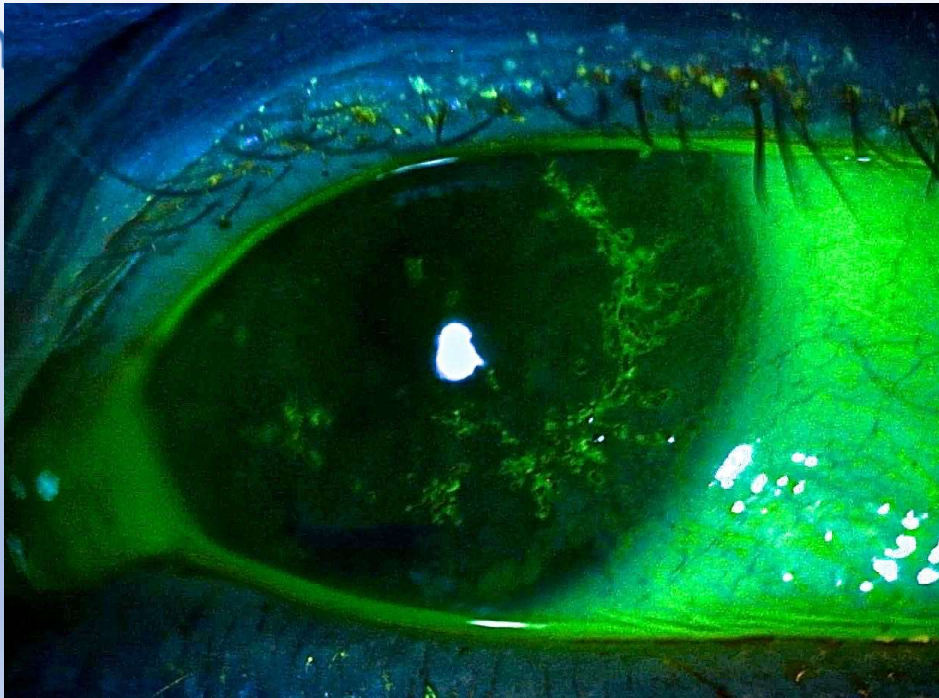
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Ep

- 48 yo WF D
- CC; Painful
- Dry Mouth,

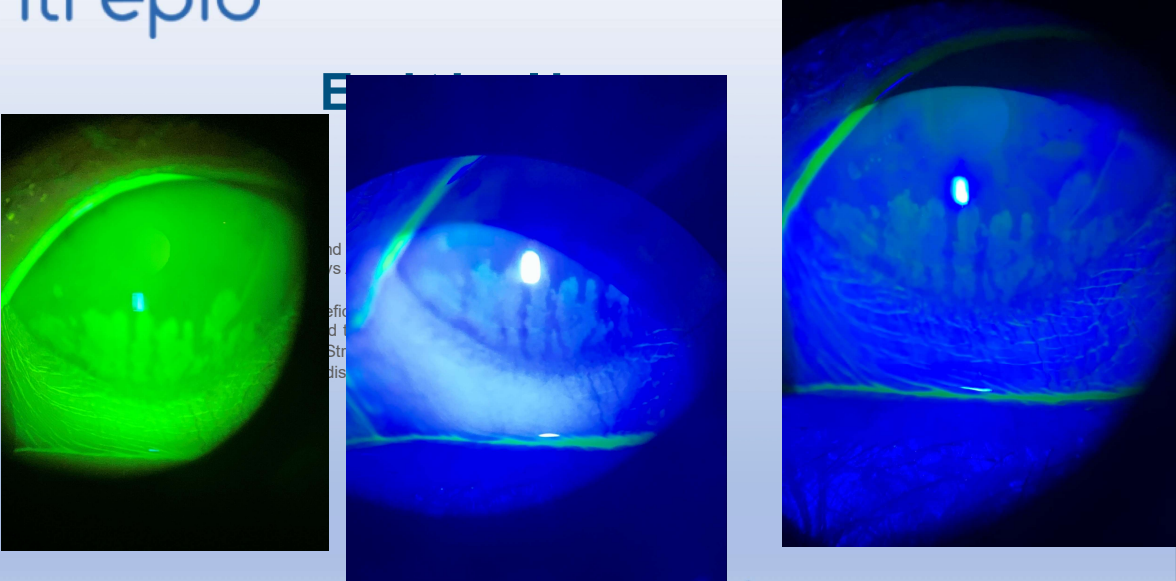



Intrepid




 Intrepid

E

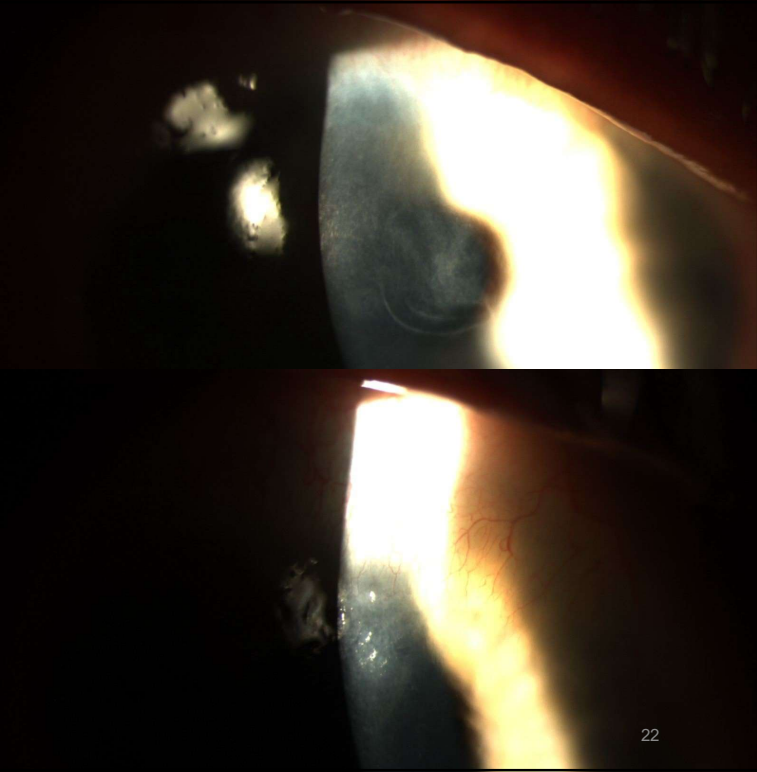


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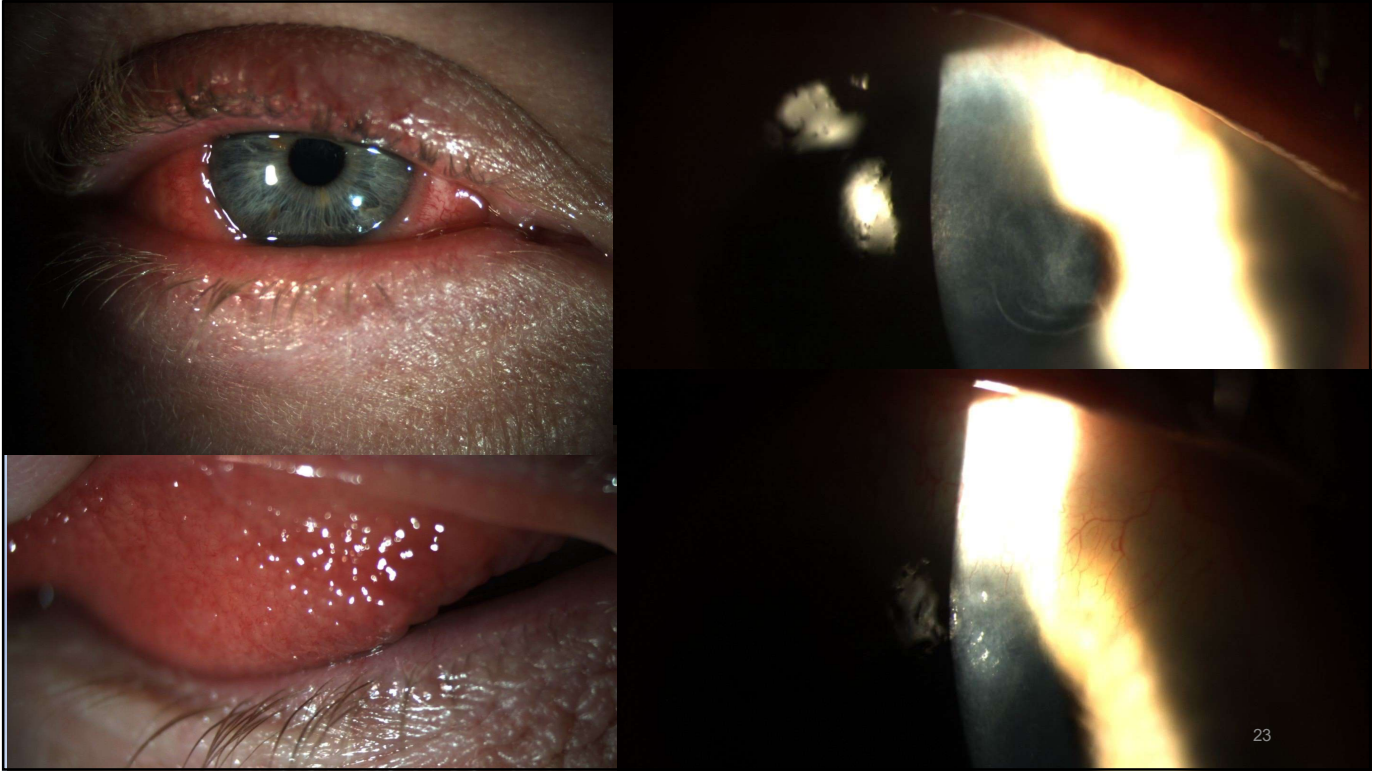
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Epithelium

- 35 yo M CC; RED, Watery, Blurry
- Superior corneal irregularity



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Case Discussion

- 47-year-old female presents with intermittent pain left eye x 9 months
- Has seen 3 previous docs who “couldn’t fix me”
- Was told she has “abrasions” on her eye
- Started a few weeks after her infant scratched her eye
- Has spent significant time in a bandage CL
- Uses Systane intermittently during day and Tobramycin ointment at night



Intrepid



Case Discussion

- *Recurrent Corneal Erosion*

- *What Treatment(s) Should We Use?*
- *Lubrication*
- *Hyperosmotics*
- *Anti-inflammatories*
- *Amniotic Membrane*
- *Procedural intervention (Stromal Puncture, Debridement, Diamond Burr Polishing, PTK)*



Bowman's Layer

- *Present below corneal basal epithelium as disorganized layer of collagen fibrils*
- *Approx 10um thick*
- *Function?*
- *Pathologies:*
- *ABMD/RCE*
- *Salzmann's*
- *Irregular astigmatism?*





Bowman's Layer

Basement Membrane

Case

ABMD & RCE
 Salzmann's Degeneration
 Direct support of the epithelium
 More common root of irregular astigmatism

Treatment Options

Debridement
 Polishing
 Contact Lenses
 Anti-inflammatory
 Medical
 Topical
 Oral
 Amniotics
 Surgical



Anterior Stroma

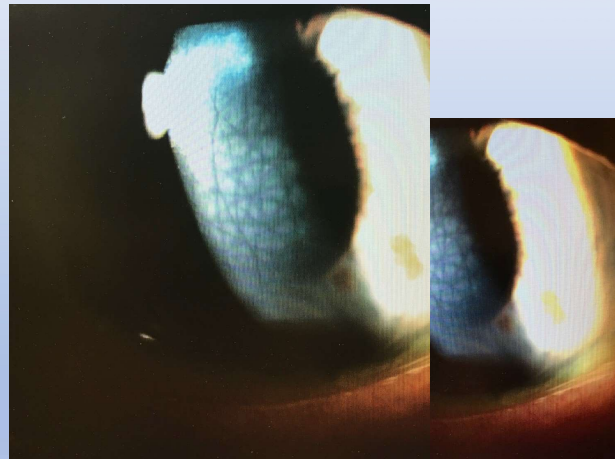
Anterior Stroma

Case

Francois vs Shagreen
 Schnyder Corneal Dystrophy (SCD)

Treatment Options

Observation
 PTK



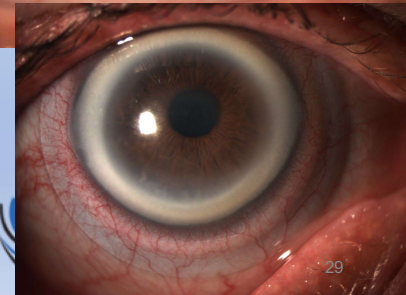
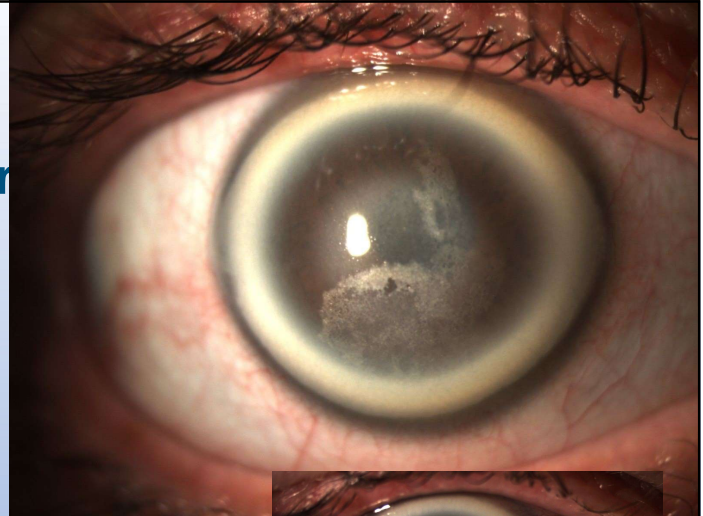


Anterior

Anterior Stroma

Case

Francois vs Shagreen
 Schnyder Corneal Dystrophy (SCD)
 Treatment Options
 Observation
 PTK



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Anterior Stroma

• Reference ICD3

IC3D Classification of Corneal Dystrophies—Edition 2

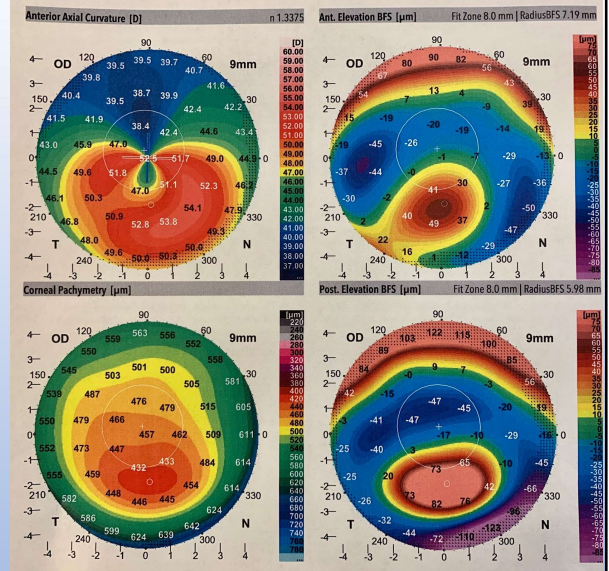
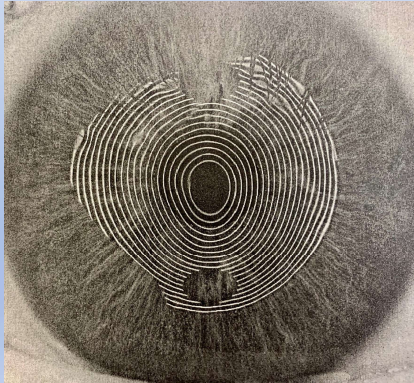
Jayne S. Weiss, MD,* Hans Ulrik Møller, MD, PhD,† Anthony J. Aldave, MD,‡ Berthold Seitz, MD,§
 Cecilie Bredrup, MD, PhD,¶ Tero Kivelä, MD, FEBO,|| Francis L. Munier, MD,**
 Christopher J. Rapuano, MD,†† Kanwal K. Nischal, MD, FRCOphth,‡‡ Eung Kweon Kim, MD, PhD,§§
 John Sutphin, MD,¶¶ Massimo Busin, MD,||| Antoine Labbé, MD,*** Kenneth R. Kenyon, MD,†††
 Shigeru Kinoshita, MD, PhD,‡‡‡ and Walter Lisch, MD§§§§



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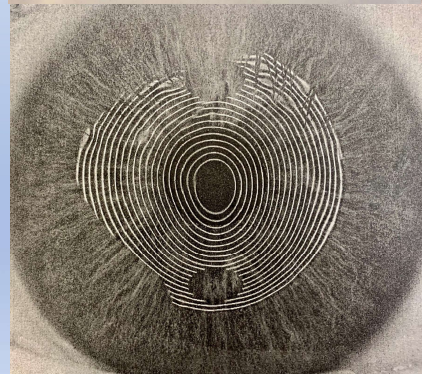
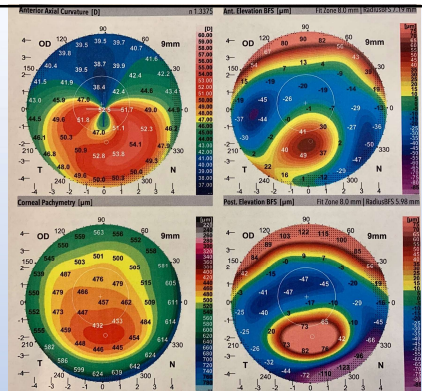


Posterior Stroma



Posterior Stroma

- What's new with Ectasia's and Keratoconus?
- CXL
- Genetic Testing
- CXL/PRK
- Contact Lenses





Posterior Stroma

12yo Male

Rx shift and decreased BCVA OS

MRx 2019

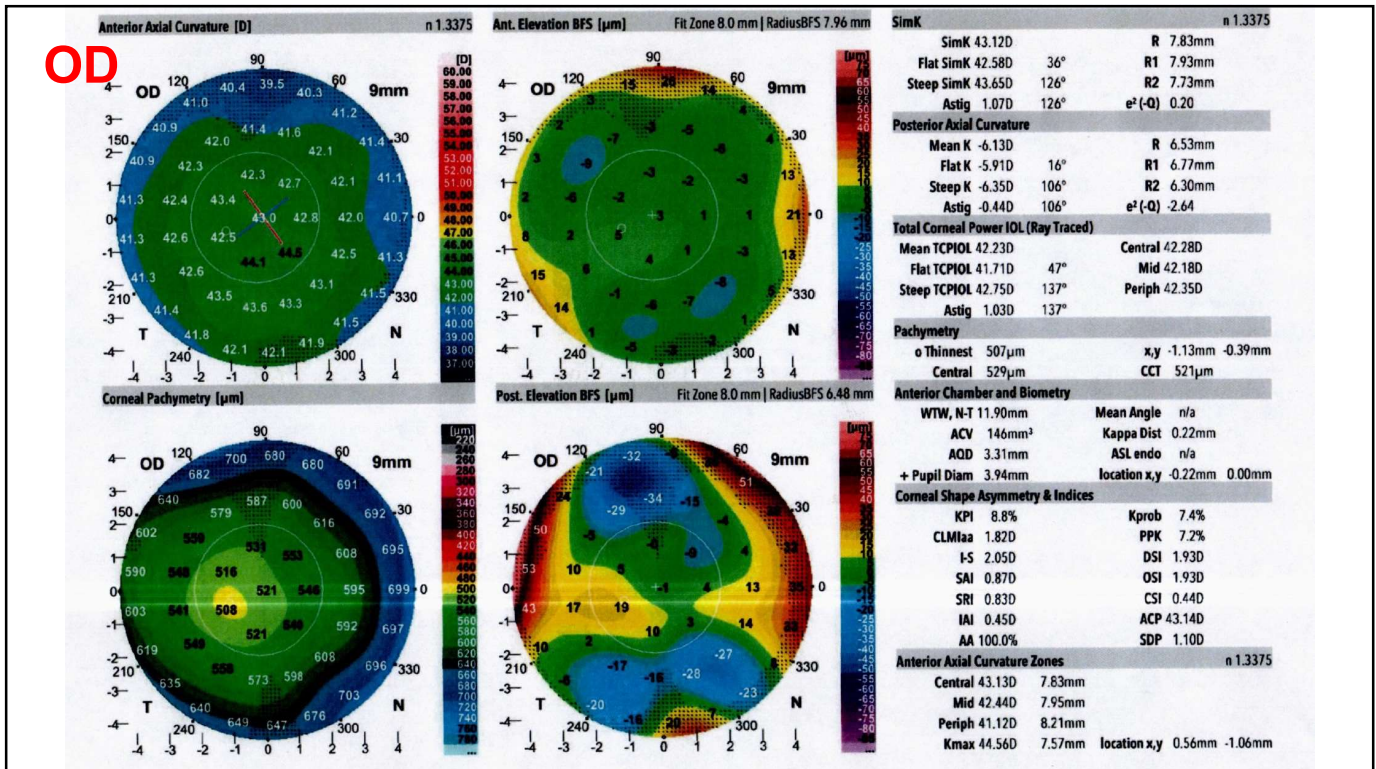
PI 20/20
PI -0.50 x120 20/20

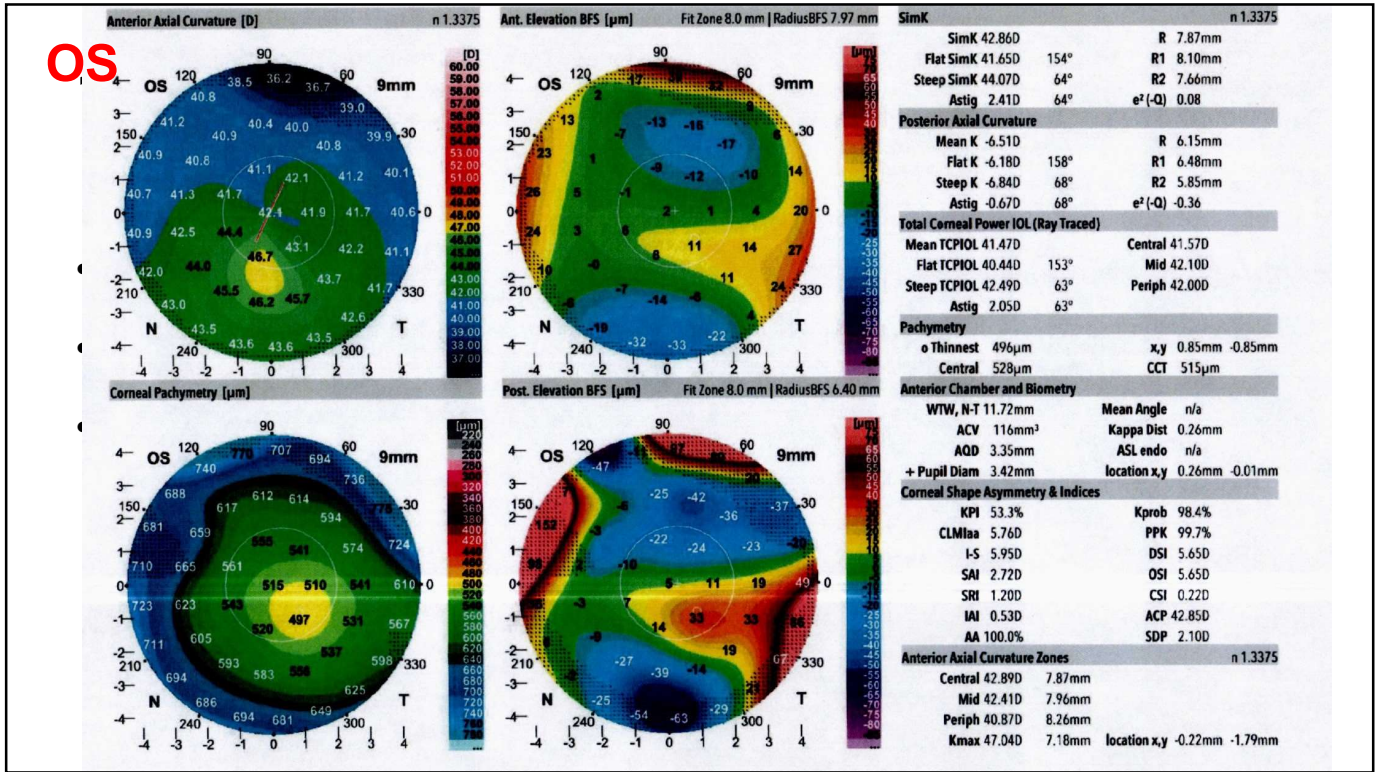
MRx 2021

PI-0.50x180 20/20
PI-1.25x 130 20/30

K's 2021

42.58/43.65
41.65/44.07





Posterior Stroma

12yo Male

Now What?

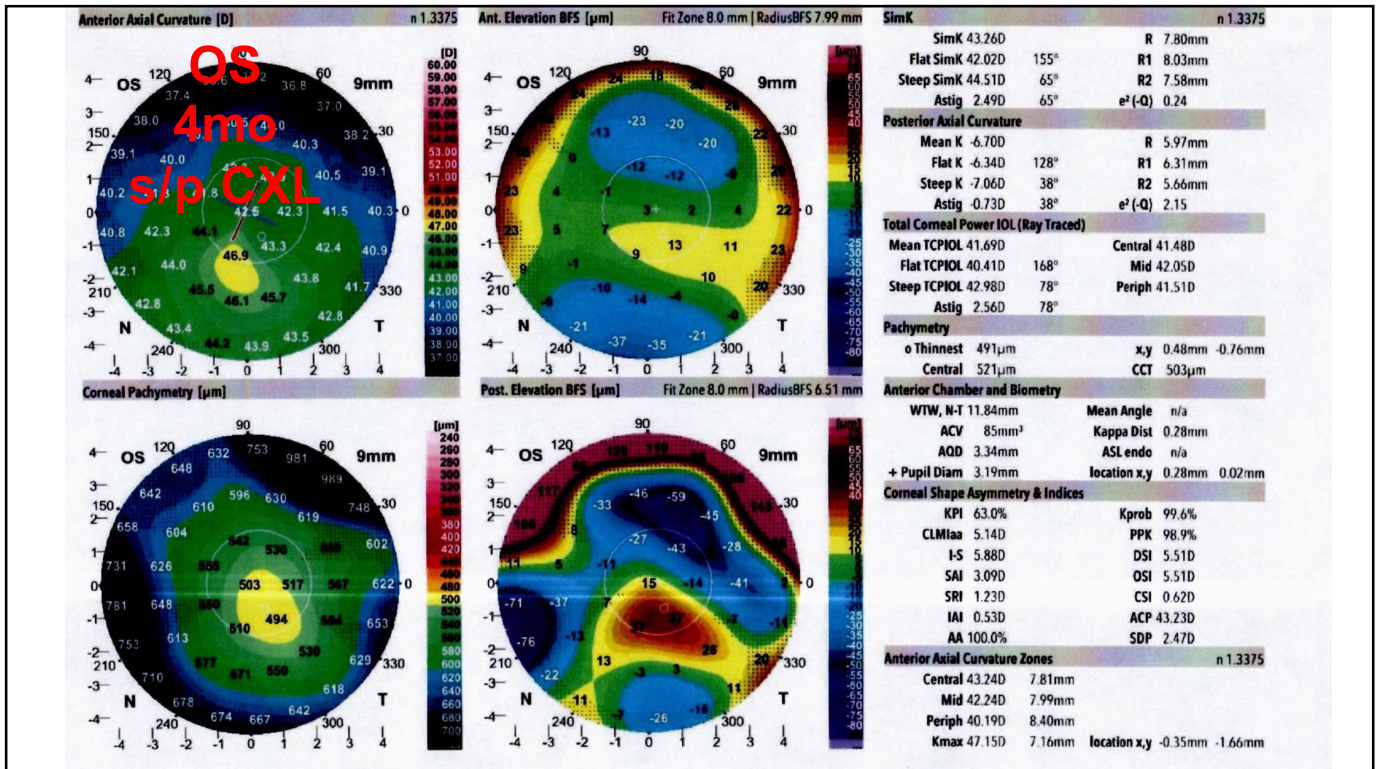
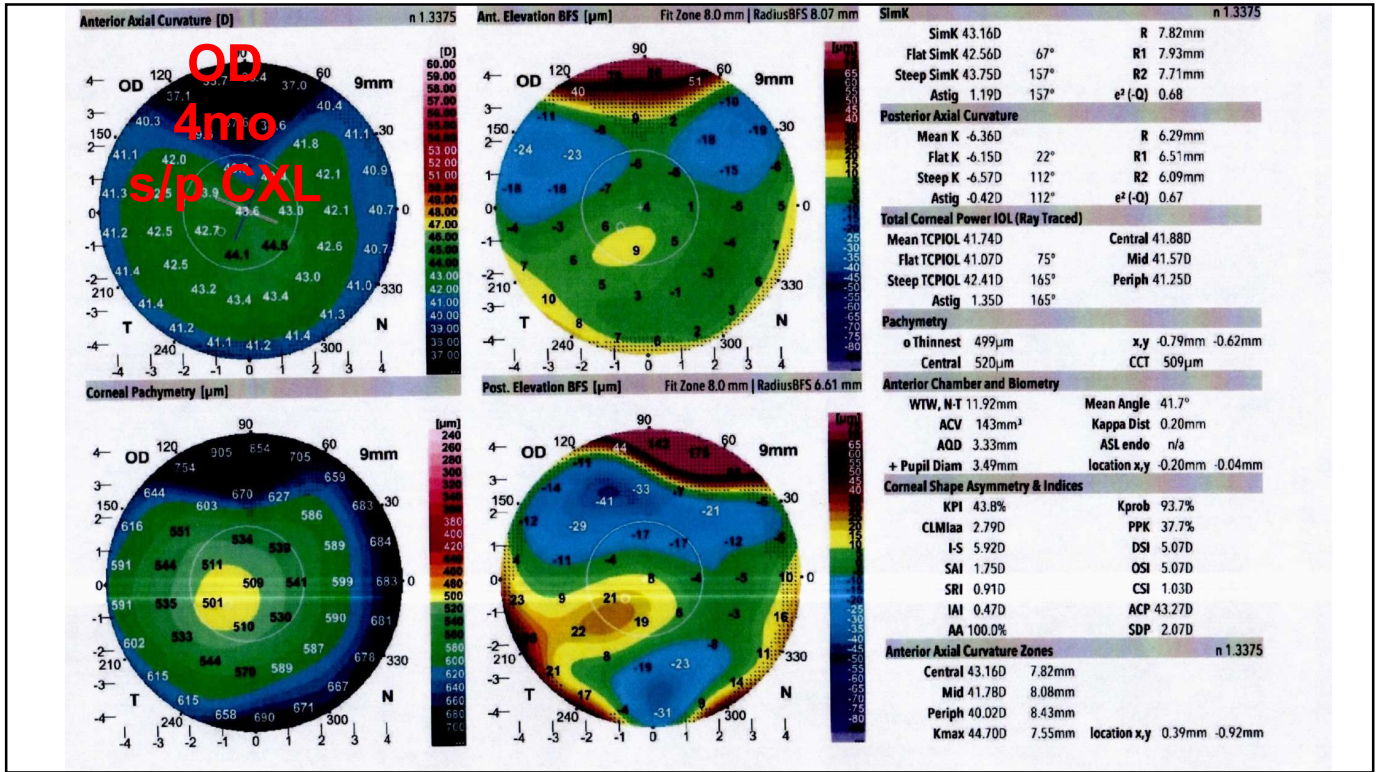
CXL?

Treat OD too?

Monocular KCN?

Other Therapies or Options







Posterior Stroma

And the Plot Thickens...

Patient has an identical twin...



Posterior Stroma

Identical Twin

Genetic Risk

Keratoconus and Genetics





Posterior Stroma

FINAL RESULTS			
CONDITION TESTED	RESULT	DETAIL	EXPLANATION
Keratoconus (KC)	High genetic risk	67 polygenic risk score	Tested for variants within 75 genes found to be associated with keratoconus.
TGFBI Corneal Dystrophies (CD)	Negative for TGFBI Corneal Dystrophies	No pathogenic variants detected	Tested Negative for 70 known variants associated with TGFBI corneal dystrophies.

This AvaGen Genetic Test result should be considered with other clinical criteria, the patient's family history and communicated in a setting that includes appropriate genetic counseling.

Keratoconus (KC) Risk Assessment

Based on the polygenic risk score of 67, this patient's risk for KC is High.



THE POLYGENIC KC RISK SCORE: The AvaGen Genetic Eye Test provides a polygenic risk score for individuals tested for their genetic risk for KC. The risk score is the cumulative sum of individual risk contributed by several independent SNPs that were identified in our genetic association study by screening thousands of variants in 75 genes related to corneal structure and function. KC is a complex genetic disease that involves genetic and environmental components as well as their interactions that contribute to the development of the disease. Genetics is an important contributor in KC risk, but it is not the only contributing factor that determines risk for KC.



Posterior Stroma

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They ARE Identical Twins!





Posterior Stroma

Keratoconus Polygenic Test Details

Keratoconus risk genes for this patient:

ABCA4, ADAMTS18, COL2A1, COL4A1, KRT3, LTBP2

Keratoconus-Related Genes Tested:

ABCA4, ABCB5, ABCG6, ADAMTS18, ADGRV1, AGBL1, ANGPLT7, BEST1, CHST6, COL2A1, COL4A1, COL4A2, COL4A3, COL4A4, COL5A1, COL5A2, COL6A1, COL6A2, COL12A1, COL17A1, CYP4V2, DIAPH1, DDOCK9, FOXE3, FYN, GJAR, GSN, HGF, IL1A, IL1RN, IL6, IL10, ITGB1, KERA, KRT3, KRT12, KRT13, KRT15, KRT16, KRT23, KRT24, LCAT, LOX, LRRN1, LTBP2, MAP2K1, MAP3K19, MTOR, MYLK, NLRP1, OVOL2, PAX6, PIK3CG, PIK3FE, PIK3R1, PRDM5, PTK2, PXDN, PXN, RAF1, RHOA, SFTPD, SHC1, SIX5, SLC4A11, TACSTD2, TCF4, TGFBI, TLN1, UBIAD1, VSX1, WNT9A, WNT9B, ZEB1, ZNF469

Corneal Dystrophy (CD) Test Result

This patient has 0 out of 70 known variants associated with TGFBI corneal dystrophies.

Corneal Dystrophy associated variants within the TGFBI gene in this patient:

Negative for a disease-causing variant, in TGFBI gene.

AvaGen Detects the Following TGFBI Associated Corneal Dystrophies

Granular Type 1	Lattice Type IIIA	Epithelial Basement Membrane
Granular Type 2	Reis-Bucklers	Schnyder's-like
Lattice Type 1	Theill-Behnke	



Posterior Stroma

Now What?

CXL for Twin?

Nature vs Nurture?

Behaviors, Habits?

Preventative Care for KCN?



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What Would YOU Do?

Treat Both Eyes, and Twin

Treat ONE eye, and NOT Twin

Treat Both Eyes, and NOT Twin

Treat ONE eye and Twin

None of the above

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Poll

- How many layers of the cornea are there?
 - 4
 - 5
 - 6
 - The same number of layers as Jean Lang's (my mom) homemade strudel



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How many layers of the cornea are there?

A

4

B

5

C

6

D

The same number of layers as Jean Lang's (my mom) homemade strudel

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Dua's Layer (6th-ish Layer)

- No relation to **Dua Lipa**
- So... How many layers of the cornea are there??? **6**
- Harminder S. Dua, MD, PhD, professor of ophthalmology and visual sciences at the University of Nottingham.
- "It's a tough, well-defined, acellular lining only about 10µm to 15µm thick, between the corneal stroma and Descemet's membrane."
- A paper published in 1991 by Perry Binder, MD, describes a network of fibers located at the interface of the posterior stroma and DM, although it was not identified as a distinct corneal layer





Dua's Layer

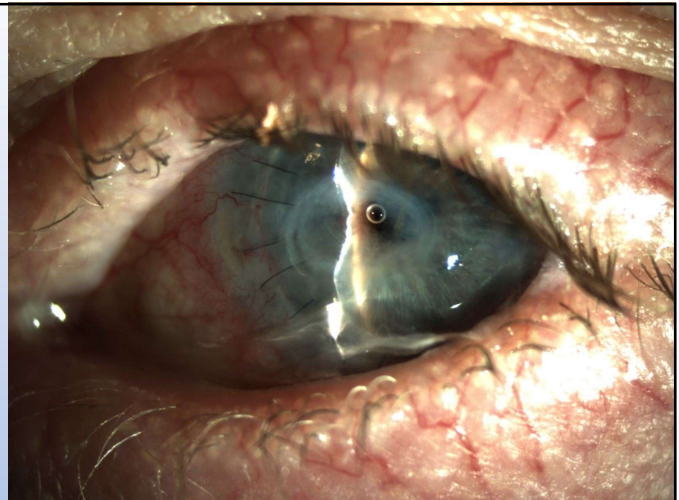
- They found that the separation of layers that yielded the strongest tissue was not between the stroma and the DM, as believed. Rather, the ideal separation was between the deep stroma and this unrecognized layer.
- Appears to be a very strong layer, maybe the strongest in the cornea for its size
- May have implications in stromal and endothelial transplants and may help describe conditions like hydrops and descemetocele



Descemet's Layer

Descemet's Case

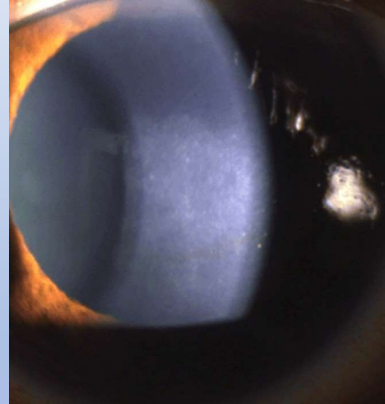
- Descemetocele
- Disease process
- Management
- Treatment Options
 - Surgical options
 - Medical therapy
 - Contact lenses
 - Glues





SGH Case

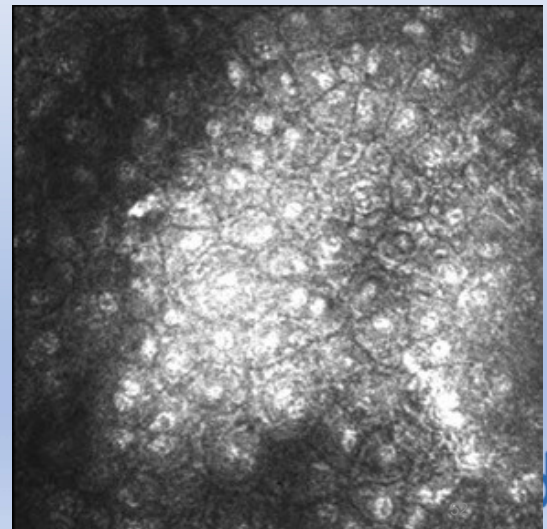
- 55 year-old female, referred for cataract surgery
- BCVA 20/30 OD, 20/25 OS
- Does not BAT worse?
- Systemic history – unremarkable
- 1-2+ NS OU on exam
- Describes “haloes” at night with oncoming headlights
- What is our approach?
- What if she had borderline/significant cataracts?



Endothelium

Endothelium Case

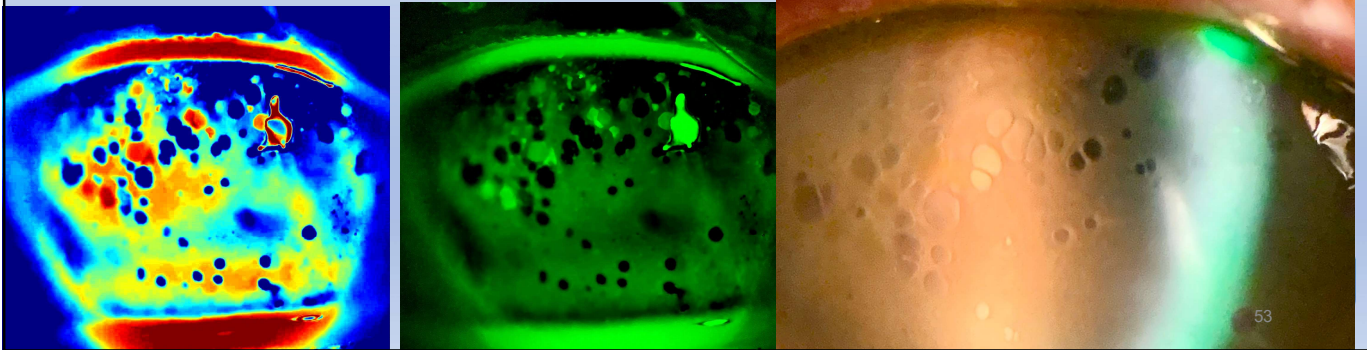
- Fuchs
- Other causes of endo loss
- MIGS
- Tubes
- Multiple Surgeries
- Treatment Options
- Rho-Kinase inhibitors as an option?
- Contact Lens
- Medical Options
- Surgical Options





Putting it all together

- *All The Layers*



Putting it all together

Remember the “WHERE and WHY”

Why this pathology, and Where it originated

HOW it interacts with the other layers, vision, other structures, and conditions

Stepwise approach

Patient specific discussion of options

Ongoing assessment if treatment is sufficient

Is compliance with treatment plan is possible and/or happening





Putting it all together

Poll: What is your favorite layer of the cornea?

- Epithelium
- Bowman's
- Stroma
- Dua's
- Descemet's
- Endothelium



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What's Your FAVORITE Corneal Layer?

Epithelium
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Descemet's
Endothelium

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Questions???

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drjakelang@gmail.com

 @SeeOneTeachOne

